The discrepancy between high pathological complete response (pCR) rate and low breast conserving surgery (BCS) following neoadjuvant therapy: analysis from the NeoALTTO trial (BIG 1-06)

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Disclosure slide

• I have no conflicts of interest to declare
Neoadjuvant therapy

- Test sensitivity to systemic therapy
- Increase breast conservation rates
- Down staging of locally-advanced disease
- Elimination of micro-metastasis
pCR is an early read-out of long-term outcome

**All Patients**

Log-rank
$P < .001$

**HER2+ BC**

Log-rank
$P < .001$

**Graphs**

- Proportion Disease Free vs Disease-Free Survival (months)
  - **All Patients**
    - ypT0 ypN0 (n = 955)
    - ypTis ypN0 (n = 309)
    - ypT0/is ypN+ (n = 186)
    - ypT1mic ypN+/- (n = 478)
    - ypT > 1mic ypN+/- (n = 4,449)
  - **HER2+ BC**
    - pCR (n = 164)
    - no pCR (n = 373)

*www.esmo2012.org*

von Minckwitz G et al; JCO 2012
“The rate of breast conserving surgery should increase in patients with complete or partial clinical response”
THE Neo-ALTTO TRIAL

Randomize

Lapatinib
Paclitaxel

Trastuzumab
Paclitaxel

Lapatinib
Trastuzumab
Paclitaxel

Surgery

pCR

24.7%

29.5%

51.3%

Breast Conservation

42.9%

38.9%

41.4%

6 weeks

+ 12 weeks

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Baselga J et al; Lancet 2012
OBJECTIVE

To investigate the different factors that affected the choice of surgery in patients enrolled in the Neo-ALTTO trial.
FACTORS EXAMINED

• Age

• Multicentricity/Multifocality

• Planned surgery at diagnosis

• Physical examination before surgery

• Imaging before surgery

• Tumor characteristics

• Geographic region
METHODS

• The analysis was performed on patients enrolled in the NeoALTTO trial, comparing the results across the treatment arms whenever possible.
• The prevalence of the different clinicopathologic (C/P) factors was compared between patients subjected and not subjected to breast conserving surgery (BCS).
• A logistic regression model relating the probability of BCS to the candidate predictors and treatment arm was performed, to discover
  • Whether any of the C/P factors is usefully predictive of BCS
  • Whether adjustment for these predictors changes the apparent relationship between treatment arm and BCS.
RESULTS
Patient Population

Neo-ALTTO Study
N = 455 patients in 23 countries

Sub-study
N = 429 evaluable patients

N = 26 patients excluded
(surgery not done)
Baseline Characteristics

**Geographics***

<table>
<thead>
<tr>
<th>Geographics</th>
<th>Developing Countries</th>
<th>Developed Countries</th>
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</thead>
<tbody>
<tr>
<td>p=0.006</td>
<td>67.9%</td>
<td>53.2%</td>
</tr>
<tr>
<td></td>
<td>32.1%</td>
<td>46.8%</td>
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</tbody>
</table>

*Developing Countries include: low, low-middle and Upper-middle income economies

*Developed Countries include: High-income economies and high-income OECD members

**Age**

<table>
<thead>
<tr>
<th>Age</th>
<th>20-&lt;40 years</th>
<th>40-&lt;50 years</th>
<th>50-&lt;60 years</th>
<th>&gt;60 years</th>
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<tbody>
<tr>
<td></td>
<td></td>
<td>58.5%</td>
<td>60.6%</td>
<td>55.7%</td>
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<tr>
<td></td>
<td>41.5%</td>
<td>39.4%</td>
<td>44.3%</td>
<td>51.2%</td>
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</tbody>
</table>

p=0.2
Baseline Characteristics

**Histological Grade**
- G1: 54.5%, 45.5%
- G2-3: 46.4%, 26.7%
- Gx: 73.3%

**Histological type**
- Lobular: 100%
- Ductal: 54.5%
- Others: 45.5%

* 17 patients only diagnosed with lobular carcinoma
Baseline Characteristics

**ER status**

- **p=0.002**

<table>
<thead>
<tr>
<th></th>
<th>not BCS</th>
<th>BCS</th>
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</thead>
<tbody>
<tr>
<td>ER+</td>
<td>49.8%</td>
<td>50.2%</td>
</tr>
<tr>
<td>ER-</td>
<td>63.1%</td>
<td>36.9%</td>
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</table>

**Multicentricity/focality**

- **p<0.0001**

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<thead>
<tr>
<th></th>
<th>not BCS</th>
<th>BCS</th>
</tr>
</thead>
<tbody>
<tr>
<td>no</td>
<td>54.1%</td>
<td>45.9%</td>
</tr>
<tr>
<td>yes</td>
<td>75%</td>
<td>25%</td>
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</tbody>
</table>
Baseline Characteristics

**Size**
- T2: 53.9% not BCS, 46.1% BCS
- T3: 31.5% not BCS, 68.5% BCS
- T4: 81% not BCS, 19% BCS

**Planned surgery**
- Not conservative: 30% not BCS, 70% BCS
- Conservative: 26% not BCS, 74% BCS

**Statistics**
- Size: p=0.0004
- Planned surgery: p<0.0001
Post Baseline Characteristics

Tumor measurement by radiology at pre-surgery visit

- CR: 53% (not BCS), 47% (BCS)
- PR: 45% (not BCS), 58% (BCS)
- SD: 55%

p=0.87

Tumor measurement by breast palpation at pre-surgery visit

- zero: 45.8% (not BCS), 67.2% (BCS)
- not zero: 54.2% (not BCS), 32.8% (BCS)
- not measured: 49%

p=0.0004
Factors Affecting the Decision for Breast Conservation After Neoadjuvant Therapy

Adjusted Logistic Regression Model (Including planned surgery at baseline) *

- Planned surgery (BCS vs. No)
- Multifocal/centric (Yes vs. No)
- Baseline TNM (T2 vs. T4)
- Baseline LN status (N0 vs. N+)
- Developed vs Developing
- ER status (-ve vs. +ve)
- Residual palpable mass (yes vs. no)

**OR (95% CI)**

More BCS

Less BCS

* No interaction according to treatment arm

The analysis was also adjusted for age, histological grade, response to treatment, completion of therapy.
Factors Affecting the Decision for Breast Conservation After Neoadjuvant Therapy

Adjusted Logistic Regression Model (Excluding planned surgery at baseline) *

- Multifocal/centric (Yes vs. No)
- Baseline TNM (T2 vs. T4)
- Baseline LN status (N0 vs. N+)
- Developed vs Developing
- ER status (-ve vs. +ve)
- Residual palpable mass (yes vs. no)

OR (95% CI)

The analysis was also adjusted for age, histological grade, response to treatment, completion of therapy.

* No interaction according to treatment arm
Conclusions

Our study suggests that the decision of surgical treatment post neoadjuvant therapy is mainly based on baseline characteristics. This was observed independent of the treatment arm and response to treatment. These factors were:

– Type of planned surgery at diagnosis
– Multicentricity/Multifocality of the tumor
– Receptor status (ER-negative less likely to receive BCS)
Conclusions

• Several factors were independently associated with the type of planned surgery at diagnosis
  – Geographic region (less BCS in developing countries)
  – Tumor size (less BCS in T3/4)

• These results call for a clear consensus on the role of BCS in patients responding to neoadjuvant therapy. This will translate the progress in neoadjuvant therapies into improved breast conservation rates
Acknowledgements

Groups, Sites and Patients

Study Principal Investigators: J. Baselga and H. Eidtmann

BIG GROUPS

- BrEAST
- GBECAM
- GECO PERU
- German ALTTO
  (AGO BREAST, GBG, NOGGO, SUCCESS, WSG & indep. sites)

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- NBCG
- NCIC-CTG
- SOLTI
- TCOG

Independent Sites

- FNCLCC
- KCSG

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